

Claims:

*Please amend the claims as follows:*

Please amend claims 5-8, 12-14, 17-22, 25-27, 30, and 31.

Please add new claims 32-48.

1. **(Original)** A method for treating a disorder in which TNF $\alpha$  activity is detrimental comprising administering to a subject an effective amount of a TNF $\alpha$  inhibitor in a low dose therapy, such that the disorder is treated.
2. **(Original)** The method of claim 1, wherein the disorder is arthritis.
3. **(Original)** The method of claim 2, wherein the disorder is rheumatoid arthritis.
4. **(Previously presented)** The method of claims 2 and 3, wherein symptoms selected from the group consisting of bone erosion, cartilage erosion, inflammation, and vascularity, are treated.
5. **(Currently amended)** The method of any one of claims 1-3 ~~1-4~~, wherein the TNF $\alpha$  inhibitor is an anti-TNF $\alpha$  antibody, or an antigen-binding portion thereof, or a TNF $\alpha$  fusion protein D2E7.
6. **(Currently amended)** The method of claims 5 ~~1-4~~, wherein the TNF $\alpha$  fusion protein ~~inhibitor~~ is etanercept. ~~Etanercept or Remicade~~.
7. **(Currently amended)** The method of claim 32, ~~claims 1-4~~, wherein D2E7 ~~the TNF $\alpha$  inhibitor~~ is administered in a low dose comprising 0.01 – 0.1 ~~2.0~~ mg/kg.
8. **(Currently amended)** A low dose method to alleviate symptoms associated with a disorder in which TNF $\alpha$  activity is detrimental, comprising administering a low dose of a TNF $\alpha$  inhibitor to a subject suffering from said disorder, such that the symptoms are treated.
9. **(Original)** The method of claim 8, wherein the disorder is arthritis.
10. **(Original)** The method of claim 9, wherein the disorder is rheumatoid arthritis.

11. **(Previously presented)** The method of claims 9 and 10, wherein symptoms are selected from the group consisting of bone erosion, cartilage erosion, inflammation, and vascularity.
12. **(Currently amended)** The method of any one of claims 8-10, ~~claims 8-11~~, wherein the TNF $\alpha$  inhibitor is an anti-TNF $\alpha$  antibody, or an antigen-binding portion thereof, or a TNF $\alpha$  fusion protein.
13. **(Currently amended)** The method of claim 12, ~~claims 8-11~~, wherein the TNF $\alpha$  fusion protein inhibitor is etanercept ~~Etanercept or Remicade~~.
14. **(Currently amended)** The method of claim 33, ~~claims 8-13~~, wherein D2E7 the TNF $\alpha$  inhibitor is administered in a low dose comprising 0.01 – 0.1 ~~2-0~~ mg/kg.
15. **(Original)** A method for treating arthritis comprising administering to a subject an effective amount of a TNF $\alpha$  inhibitor in a low dose therapy, such that the arthritis is treated.
16. **(Original)** The method of claim 15, wherein the arthritis is rheumatoid arthritis.
17. **(Currently amended)** The method of ~~claims~~ either claim 15 or and 16, wherein arthritis is treated by alleviating symptoms selected from the group consisting of bone erosion, cartilage erosion, inflammation, and vascularity.
18. **(Currently amended)** The method of claim 15 or 16 ~~claims 14-17~~ wherein the TNF $\alpha$  inhibitor is an anti-TNF $\alpha$  antibody, or an antigen-binding portion thereof, or a TNF $\alpha$  fusion protein ~~D2E7~~.
19. **(Currently amended)** The method of claim 18 ~~claims 14-17~~ wherein the TNF $\alpha$  fusion protein inhibitor is etanercept ~~Etanercept or Remicade~~.
20. **(Currently amended)** The method of claim 34, ~~claims 15-19~~, wherein the TNF $\alpha$  inhibitor D2E7 is administered at a low dose comprising 0.01 – 0.1 ~~2-0~~ mg/kg.

21. **(Currently amended)** A low dose method for treating symptoms associated with arthritis comprising administering to a subject a low dose of an effective amount of a TNF $\alpha$  inhibitor, such that the symptoms are alleviated.
22. **(Currently amended)** The method of claim 21, wherein the arthritis is rheumatoid arthritis.
23. **(Previously presented)** The method of claims 21 and 22, wherein the symptoms are selected from the group consisting of bone erosion, cartilage erosion, inflammation, and vascularity.
24. **(Original)** The method of claim 23, wherein the symptoms are further selected from the group consisting of joint distortion, swelling, joint deformation, ankylosis on flexion, and severely impaired movement.
25. **(Currently amended)** The method of claims 21 or 22 ~~claims 21-24~~, wherein the TNF $\alpha$  inhibitor is an anti-TNF $\alpha$  antibody, or an antigen-binding portion thereof, or a TNF $\alpha$  fusion protein ~~D2E7~~.
26. **(Currently amended)** The method of claim 25 ~~claims 21-24~~, wherein the TNF $\alpha$  inhibitor fusion protein ~~inhibitor~~ is etanercept ~~Etanercept or Remicade~~.
27. **(Currently amended)** The method of claim 35, ~~claims 21-26~~, wherein D2E7 ~~the TNF $\alpha$  inhibitor~~ is administered at a low dose comprising 0.01 – 0.1 ~~2-0~~ mg/kg.
28. **(Original)** A method of sequestering TNF $\alpha$  into complexes in a subject suffering from a disorder in which TNF $\alpha$  activity is detrimental, by administering a low dose of a TNF $\alpha$  inhibitor to the subject.
29. **(Original)** The method of claim 28, wherein the serum level of TNF $\alpha$  is higher than the serum level of TNF $\alpha$  in a subject not suffering from a disorder in which TNF $\alpha$  activity is detrimental.
30. **(Currently amended)** The method of claims 28 ~~29~~, wherein the anti-TNF $\alpha$  inhibitor is an anti-TNF $\alpha$  antibody, or an antigen-binding portion thereof, or a TNF $\alpha$  fusion protein ~~D2E7~~.

31. **(Currently amended)** The method of any one of claims 1, 8, or 15 ~~1-30~~, wherein the TNF $\alpha$  inhibitor is administered with an additional therapeutic agent.
32. **(New)** The method of claim 5, wherein the anti-TNF $\alpha$  antibody, or an antigen-binding portion thereof, is either infliximab or D2E7.
33. **(New)** The method of claim 12, wherein the anti-TNF $\alpha$  antibody, or an antigen-binding portion thereof, is either infliximab or D2E7.
34. **(New)** The method of claim 18, wherein the anti-TNF $\alpha$  antibody, or an antigen-binding portion thereof, is either infliximab or D2E7.
35. **(New)** The method of claim 25, wherein the anti-TNF $\alpha$  antibody, or an antigen-binding portion thereof, is either infliximab or D2E7.
36. **(New)** The method of claim 30, wherein the anti-TNF $\alpha$  antibody, or an antigen-binding portion thereof, is either infliximab or D2E7.
37. **(New)** The method of claim 30, wherein the TNF $\alpha$  fusion protein is etanercept.
38. **(New)** The method of claim 6, wherein etanercept is administered in a low dose comprising 0.01 - 1.0 mg/kg.
39. **(New)** The method of claim 32, wherein infliximab is administered in a low dose comprising 0.01 - 0.5 mg/kg.
40. **(New)** The method of claim 5, wherein the anti-TNF $\alpha$  antibody, or an antigen-binding portion thereof, is human.
41. **(New)** The method of claim 40, wherein the anti-TNF $\alpha$  antibody, or antigen-binding portion thereof, dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $IC_{50}$  of  $1 \times 10^{-7}$  M or less.
42. **(New)** A low dose method for treating rheumatoid arthritis in which TNF $\alpha$  activity is detrimental comprising administering to a subject a low dose of a

human TNF $\alpha$  antibody, or an antigen-binding portion thereof, such that the disorder is treated.

43. (New) The method of claim 36, wherein symptoms selected from the group consisting of bone erosion, cartilage erosion, inflammation, and vascularity, are treated.

44. (New) The method of claim 36, wherein the anti-TNF $\alpha$  antibody, or antigen-binding portion thereof, dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $IC_{50}$  of  $1 \times 10^{-7}$  M or less.

45. (New) The method of claim 36, wherein the anti-TNF $\alpha$  antibody, or antigen-binding portion thereof, is D2E7.

46. (New) The method of claim 36, wherein the amount of antibody, or antigen-binding portion thereof, administered to the subject comprises 0.01 – 0.1 mg/kg.

47. (New) The method of any one of claims 1, 8, 15, or 21, wherein the amount of anti-TNF $\alpha$  antibody, or an antigen-binding portion thereof, administered to the subject comprises 0.01 – 0.1 mg/kg.

48. (New) A low dose method of improving symptoms in the joints of a subject having arthritis comprising administering to the subject a low dose of a human anti-TNF $\alpha$  antibody, or antigen-binding portion thereof, comprising 0.01-0.1 mg/kg such that at least one symptom selected from the group consisting of inflammation, cartilage erosion, bone erosion, and vascularity is improved.

49. (New) The method of claim 44, wherein the anti-TNF $\alpha$  antibody, or antigen-binding portion thereof, is D2E7.